Applicants: BACOPOULOS et al. Attorney Docket No: 24852-502 NATL

Int'l Appl. No.: PCT/US2004/026161

## **Amendments to the Claims:**

This listing of claims will replace all prior versions and listings of claims in the application:

## **Listing of Claims:**

1. (Currently amended) A method of treating cancer in a subject in need thereof, comprising the step of administering to the subject a first amount of suberoylanilide hydroxamic acid (SAHA) or a pharmaceutically acceptable salt or hydrate thereof, represented by the structure:

in a first treatment procedure, or a pharmaceutically acceptable salt or hydrate thereof, and a second amount of an anti-cancer agent, in a second treatment procedure, wherein the first and second amounts together comprise a therapeutically effective amount thereby treating the cancer.

2. (Original) The method of claim 1, wherein said anti-cancer agent is a histone deacetylase (HDAC) inhibitor, an alkylating agent, an antibiotic agent, an antimetabolic agent, a hormonal agent, a plant-derived agent, an anti-angiogenic agent, a differentiation inducing agent, a cell growth arrest inducing agent, an apoptosis inducing agent, a cytotoxic agent, a biologic agent, a gene therapy agent, or any combination thereof.

## 3. - 14. (Cancelled).

- 15. (Currently amended) The method of claim 1, wherein the anti-cancer agent is an alkylating agent selected from the group consisting of bischloroethylamines, aziridines, alkyl alkone sulfonates, nitrosoureas, nonclassic alkylating agents, and platinum compounds, and carboplatin.
- 16. (Currently amended) The method of claim 1, wherein the anti-cancer agent is an antibiotic agent selected from the group consisting of irenotecan, doxorubicin, daunorubicin,

Applicants: BACOPOULOS et al. Attorney Docket No: 24852-502 NATL

Int'l Appl. No.: PCT/US2004/026161

epirubicin, idarubicin and anthracenedione, mitomycin C, bleomycin, dactinomycin, and

plicatomycin.

17. (Currently amended) The method of claim 1, wherein the anti-cancer agent is an

antimetabolic agent selected from the group consisting of floxuridine, fluorouracil, methotrexate,

leucovorin, hydroxyurea, thioguanine, mercaptopurine, cytarabine, pentostatin, fludarabine

phosphate, cladribine, asparaginase, capecitabine, and gemcitabine.

18. (Original) The method of claim 17, wherein said antimetabolic agent is gemcitabine.

19. (Currently amended) The method of claim 1, wherein the anti-cancer agent is an

hormonal agent selected from the group consisting of an estrogen, a progestogen, an antiesterogen, an

androgen, an antiandrogen, an LHRH analogue, an aromatase inhibitor, diethylstibestrol, tamoxifen,

toremifene, fluoxymesterol, raloxifene, bicalutamide, nilutamide, flutamide, aminoglutethimide,

tetrazole, ketoconazole, goserelin acetate, leuprolide, megestrol acetate, and mifepristone.

20. (Original) The method of claim 1, wherein the anti-cancer agent is a plant-derived agent

selected from the group consisting of vincristine, vinblastine, vindesine, vinzolidine, vinorelbine,

etoposide teniposide, paclitaxel and docetaxel.

21. (Currently amended) The method of claim 1, wherein the anti-cancer agent is a biologic

agent is selected from the group consisting of immuno-modulating proteins, monoclonal antibodies

against tumor antigens, tumor suppressor genes, and cancer vaccines.

22. (Currently amended) The method of claim 21, wherein the biologic agent immuno-

modulating protein is selected from the group consisting of trastuzumab, interleukin 2, interleukin 4,

interleukin 12, interferon El interferon D, interferon alpha, erythropoietin, granulocyte-CSF,

granulocyte, macrophage-CSF, bacillus Cahnette-Guerin, levamisole, and octreotide.

23. (Original) The method of claim 21, wherein the tumor suppressor gene is selected from

the group consisting of DPC-4, NF-1, NF-2, RB, p53, WTl, BRCA, and BRCA2.

3

Applicants: BACOPOULOS et al. Attorney Docket No: 24852-502 NATL Int'l Appl. No.: PCT/US2004/026161

24. - 32. (Cancelled).

33. (Original) The method of claim 1, wherein said anti-cancer agent is administered orally, parenterally, intraperitoneally, intravenously, intraarterially, transdermally, sublingually, intramuscularly, rectally, transbuccally, intranasally, liposomally, via inhalation, vaginally, intraoccularly, via local delivery by catheter or stent, subcutaneously, intraadiposally, intraarticularly,

34. (Original) The method of claim 1, wherein SAHA is administered orally in a pharmaceutical composition comprising SAHA and a pharmaceutically acceptable carrier or diluent.

35. - 49. (Cancelled).

intrathecally, or in a slow release dosage form.

50. (Original) The method of claim 1, wherein the cancer is selected from the group consisting of a leukemia, a lymphoma, a myeloma, a sarcoma, a carcinoma, a solid tumor or any combination thereof.

51. (Currently amended) The method of claim 1, wherein the cancer is selected from the group consisting of cutaneous T-cell lymphoma (CTCL), noncutaneous peripheral T-cell lymphoma, lymphoma associated with human T-cell lymphotrophic virus (HTLV), adult T-cell leukemia/lymphoma (ATLL), mycosis fungoides, acute leukemia, chronic leukemia, hairy cell leukemia, acute lymphocytic leukemia, acute nonlymphocytic leukemia, chronic lymphocytic leukemia, chronic myelogenous leukemia, Hodgkin's disease, non-Hodgkin's lymphoma, multiple myeloma, mesothelioma, childhood solid tumors, such as-pediatric brain neuroblastoma, pediatric retinoblastoma, rhabdomyosarcoma, Wilms' tumor, bone cancer and soft-tissue sarcomas, common solid tumors of adults, such as head and neck cancers, lung tumors, breast tumors, colon tumors, prostate tumors, bladder tumors, rectal tumors, brain tumors, endometrial tumors, (e.g., oral cancer, laryngeal cancer, and esophageal cancer, genito urinary cancers, (e.g., prostate cancer, bladder cancer, renal cancer, uterine cancer, endometrial cancer, ovarian cancer, testicular cancer, rectal cancer, and colon cancer), lung cancer, non-small cell lung cancer, breast cancer, pancreatic cancer,

Attorney Docket No: 24852-502 NATL

Applicants: BACOPOULOS et al. Int'l Appl. No.: PCT/US2004/026161

melanoma, malignant melanoma, and other skin cancers, gastric cancer, stomach cancer, brain cancer, liver cancer, adrenal cancer, kidney cancer, thyroid cancer, cancers with leukocyte infiltration of the skin or organs, breast carcinoma, cervical carcinoma, ovarian carcinoma, testicular carcinoma, lung carcinoma, bladder carcinoma, renal carcinoma, colon carcinoma, rectal carcinoma, colorectal carcinoma, stomach carcinoma, liver carcinoma, pancreatic carcinoma, basal cell carcinoma, squamous cell carcinoma of both ulcerating and papillary type, metastatic skin carcinoma, medullary carcinoma, osteo sarcoma, Ewing's sarcoma, veticulum cell sarcoma, Kaposi's sarcoma, meningioma, neuroblastoma, glioblastoma, and retinoblastoma.

106. (Currently amended) A method of selectively inducing terminal differentiation of neoplastic cells in a subject and thereby inhibiting proliferation of said cells in said subject, said method comprising the step of administering to said subject a first amount of suberoylanilide hydroxamic acid (SAHA) or a pharmaceutically acceptable salt or hydrate thereof, represented by the structure:

in a first treatment procedure, or a pharmaceutically acceptable salt or hydrate thereof, and a second amount of an anti-cancer agent, in a second treatment procedure, wherein the first and second amounts together comprise an amount effective to thereby inducing induce terminal differentiation of said cells.

109. (Currently amended) An *in-vitro* method of selectively inducing terminal differentiation of neoplastic cells and thereby inhibiting proliferation of said cells, said method comprising the step-of-contacting the cells with a first amount of suberoylanilide hydroxamic acid (SAHA) or a pharmaceutically acceptable salt or hydrate thereof, represented by the structure:

Applicants: BACOPOULOS et al. Attorney Docket No: 24852-502 NATL

Int'l Appl. No.: PCT/US2004/026161

ŀ

or a pharmaceutically acceptable salt or hydrate thereof, and a second amount of an anticancer agent, wherein the first and second amounts together comprise an amount effective to thereby inducing induce-terminal differentiation of said cells.

110. - 111. (Cancelled).

112. (New) A pharmaceutical composition comprising a first amount of suberoylanilide hydroxamic acid (SAHA) represented by the structure:

or a pharmaceutically acceptable salt or hydrate thereof, and a second amount of an anticancer agent.